1587-015-0 FWC I

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

IN RE APPLICATION OF:	:	
TETSUJI SUDOH ET AL	:	EXAMINER: LEGUYADER
SERIAL NO: 08/192,800	:	
FILED: FEBRUARY 7, 1994	:	GROUP ART UNIT: 1805
FOR: PHYSIOLOGICALLY ACTIVE POLYPEPTIDE AND DNA	:	

DECLARATION UNDER 37 C.F.R. 1.132

HONORABLE COMMISSIONER OF PATENTS & TRADEMARKS
WASHINGTON, D.C. 20231

SIR:

Now comes Tetsuji SUDOH, who declares and states that:

1. I am a graduate of Gumma University in the year 1973 and received my PH.D. degree in pharmacology from Tokyo University in the year 1992.

2. I have been employed by Daiichi Pure Chemicals Co., Ltd. for 21 years as a researcher in the field of chemical and biochemical.

3. I have read the above-identified application, the Official Actions of April 21, 1994, October 6, 1993, January 22, 1993, July 30, 1991 and February 13, 1991, the references cited therein, the Amendments filed June 13, 1991, December 30, 1991, July 21, 1993, and the Preliminary Amendment filed February 7, 1994.

4. I understand that the present invention concerns:

a cDNA consisting essentially of a base sequence encoding a polypeptide having one of the following amino acid sequences:

(1) H-Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His-OH;

(2) H-Gly Ser Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His-OH;

(3) Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val Leu Arg Arg His;

(4) His Pro Leu Gly Ser Pro Gly Ser Ala Ser Asp Leu Glu Thr Ser Gly Leu Gln Glu Gln Arg Asn His Leu Gln Gly Lys Leu Ser Glu Leu Gln Val Glu Gln Thr Ser Leu Glu Pro Leu Gln Glu Ser Pro Arg Pro Thr Gly Val Trp Lys Ser Arg Glu Val Ala Thr Glu Gly Ile Arg Gly His Arg Lys Met Val Leu Tyr Thr Leu Arg Ala Pro Arg Ser Pro Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu; and

(5) Met Asp Pro Gln Thr Ala Pro Ser Arg Ala Leu Leu Leu Leu Leu Phe Leu His Leu Ala Phe Leu Gly Gly Arg Ser His Pro Leu Gly Ser Pro Gly Ser Ala Ser Asp Leu Glu Thr Ser Gly Led Gln Glu Gln Arg Asn His Leu Gln Gly Lys Leu Ser Glu Leu Gln Val Glu Gln Thr Ser Leu Glu Pro Leu Gln Glu Ser Pro Arg Pro Thr Gly Val Trp Lys Ser Arg Glu Val Ala Thr Glu Gly Ile Arg Gly His Arg

Lys Met Val Leu Tyr Thr Leu Arg Ala Pro Arg Ser Pro
Lys Met Val Gln Gly Ser Gly Cys Phe Gly Arg Lys Met
Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly Cys Lys Val
Leu Arg Arg His;

a recombinant DNA sequence comprising a base sequence encoding one or more of polypeptides (1)-(5) above; and

a method of producing cDNA, comprising:

hybridizing a probe having a DNA sequence encoding a part of porcine brain natriuretic peptide to a human cDNA library;

selecting a positive clone; and

isolating the cDNA of the positive clone.

5. Neither the 70% degree of homology between human atrial natriuretic peptide (hANP) and porcine BNP (pBNP) taught by Sudoh et al (*Biochem. Biophys. Res. Comm.*, 155:726-732 and *Nature*, 332:78-80) nor the 50.6-65.7% degree of homology between hANP mRNA and pBNP mRNA taught by Maekawa et al is sufficiently high for one of ordinary skill to reasonably expect success in cloning and isolating the cDNA of one based on the sequence of the other.

6. Further, Table 1 of Oikawa et al teaches that the homology between hANP and other mammalian ANPs is only 52-60%. Thus, assuming that one of ordinary skill expects the same degree of homology between hBNP and other mammalian BNPs as is observed between hANP and other mammalian ANPs, Sudoh et al (*Biochem. Biophys. Res. Comm.*, 155:726-732 and *Nature*, 332:78-

80), Maekawa et al and Oikawa et al appear to indicate that the degree of homology is greater between pBNP and hANP than what one expects between pBNP and hBNP. As a result, one might expect a probe based on the pBNP gene to lead to cloning of a hANP gene, rather than a hBNP gene.

7. Sudoh et al (*Biochem. Biophys. Res. Comm.*, 159:1427-1434, attached hereto and incorporated herein by reference) disclose that human and porcine ANP's have 89.7% and 100% identical residues in the pro-form and α-form, respectively (page 1433, lines 1-3). However, the high homology between the pro- and α-forms of hANP and pANP would lead one to reasonable expect success in cloning and isolating hBNP cDNA using a 10-20 bp pBNP probe, which the present Inventors attempted but failed to successfully carry out.

8. Furthermore, the low homology (70.0%) between human prepro-BNP and porcine prepro-BNP (results determined by the present Inventors, disclosed by Sudoh et al [*Biochem. Biophys. Res. Comm.*, 159:1427-1434]) presents a sharp contrast to the more highly conserved mammalian ANP's, thus introducing an unexpected problem in cloning hBNP. This unexpected problem makes it surprising that hBNP cDNA could be cloned and isolated, given the level of ordinary skill and the knowledge in the art at the time of filing grandparent U.S. application Serial No. 07/486,827 (March 1, 1990).

9. The undersigned petitioner declares further that all statements made herein of his own knowledge are true and that

all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

10. Further declarant saith not.

Tetsuji Sudoh
Signature

October 12, 1994
Date